2009 H1N1 Influenza
Updated Key Points
December 11, 2009

What's New and Updated

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- Effectiveness of Antiviral Drugs in Reducing Influenza Associated Illness and the Risk of Severe Complications
- 2009 H1N1 Influenza Vaccine
- 2009 H1N1 Influenza Vaccine Safety
- Seasonal Influenza Vaccine

A Summary of CDC Key Public Health Messages this Season

- During the week of November 29 – December 5, 2009, flu activity continued to decline in the United States as reported in FluView. The number of states reporting widespread flu activity decreased from 25 to 14. Visits to doctors for influenza-like illness and flu-associated hospitalizations declined from the previous week; however, flu-associated deaths increased.

- Influenza is unpredictable—flu activity may continue for several weeks and it's possible that other waves of influenza may occur caused by either 2009 H1N1 viruses or regular seasonal flu viruses.

- CDC recommends a three-step approach to fighting the flu:
    - vaccination;
    - everyday preventive actions, including covering coughs and sneezes, frequent hand washing, and staying home when sick;
    - and the correct use of antiviral drugs if your doctor recommends them.

- Supplies of 2009 H1N1 vaccine continue to increase. More doses are expected for shipment each week. We ask members of the public who want to receive this vaccine to be patient as this program expands and more vaccine becomes available.

- It's very important that antiviral drugs be used early to treat flu in people who are very sick (for example people who are in the hospital) and people who are sick with flu and have a greater chance of getting serious flu complications, like people with asthma, diabetes or people who are pregnant.

Activity Update

- Each week CDC analyzes information about influenza disease activity in the United States and publishes findings of key flu indicators in a report called FluView.

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- Information collected during the week of November 29 – December 5, 2009, is being reported in FluView on December 11, 2009.
- Below is a summary of the most recent key indicators:
- Visits to doctors for influenza-like illness (ILI) nationally decreased again this week over last week. This is the sixth consecutive week of national decreases in ILI after four consecutive weeks of sharp increases. While ILI has declined, visits to doctors for influenza-like illness remain elevated nationally.
- Influenza hospitalization rates have decreased across all age groups but remain higher than expected for this time of year. Though declining, hospitalization rates continue to be highest in children 0-4 years old.
- The proportion of deaths attributed to pneumonia and influenza (P&I) based on the 122 Cities Report increased over the previous week and has been higher than expected for ten consecutive weeks.
- In addition, 16 flu-related pediatric deaths were reported this week: 13 of these deaths were associated with laboratory confirmed 2009 H1N1, 2 were associated with influenza A viruses that were not subtyped and one was associated with a seasonal influenza B virus.
- Since April 2009, CDC has received reports of 267 laboratory-confirmed pediatric deaths: 224 due to 2009 H1N1, 41 pediatric deaths that were laboratory confirmed as influenza, but the flu virus subtype was not determined, and two pediatric deaths were associated with seasonal influenza viruses. Laboratory-confirmed deaths are thought to represent an undercount of the actual number. CDC has provided estimates about the number of 2009 H1N1 cases and related hospitalizations and deaths. The increase in the proportion of deaths as other indicators are going down is not surprising as the occurrence and reporting of deaths usually lags behind that of other indicators.
- A table showing reports of flu-related pediatric deaths (including a cumulative total of 2009 H1N1 pediatric deaths since April, 2009) is available on the CDC website at http://www.cdc.gov/h1n1flu/updates/us/#pedh1n1cases .
- Since CDC began tracking pediatric flu-related deaths in 2003-2004, the number of pediatric deaths reported to CDC has ranged from 46 during the 2005-2006 season to the 204 deaths reported so far during the 2009-2010 season.
- Fourteen states are reporting widespread influenza activity; a decline of 11 states from last week. They are: Alabama, Alaska, Arizona, California, Connecticut, Delaware, Kentucky, Maine, New Hampshire, New Jersey, New York, Rhode Island, Vermont, and Virginia

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- Almost all of the influenza viruses identified so far continue to be 2009 H1N1 influenza A viruses.

- These viruses remain similar to the virus chosen for the 2009 H1N1 vaccine, and remain susceptible to the antiviral drugs oseltamivir and zanamivir with rare exception.

International Situation Update

- The 2009 H1N1 influenza virus is the predominant influenza virus in circulation worldwide.
- In temperate regions of the Southern Hemisphere, sporadic cases of 2009 H1N1 have been reported in recent weeks but no sustained transmission has been observed.
    - The epidemiology and severity of disease caused by 2009 H1N1 influenza in the Southern Hemisphere during its winter months in 2009 was very similar to what was described in the United States in the spring of 2009.
- In tropical regions of the Americas and Asia, influenza activity due to 2009 H1N1 remains variable.
- In temperate regions of the Northern Hemisphere, influenza-like illness (ILI) activity due to 2009 H1N1 has passed its highest peak in North America and in parts of Western, Northern, and Eastern Europe, but activity continues to increase in parts of Central and Southeastern Europe, as well as in South and East Asia.
- According to the World Health Organization (WHO), the majority of 2009 H1N1 influenza isolates tested worldwide remain sensitive to oseltamivir, an antiviral medicine used to treat influenza disease. Worldwide, 102 2009 H1N1 isolates tested have been found to be resistant to oseltamivir – 29 of these isolates were detected in the United States.
- The World Health Organization (WHO) continues to report updated 2009 H1N1 flu-associated laboratory-confirmed cases and deaths on its Web page (http://www.who.int/csr/disease/swineflu/updates/en/). These laboratory-confirmed cases represent a substantial underestimation of total cases in the world, as many countries focus surveillance and laboratory testing only on people with severe illness.
- For the most recent week in which data are available (November 22 to November 28, 2009) more than 89.4% of influenza specimens reported to WHO were 2009 H1N1.

- On September 17, 2009, several countries including the United States announced plans to donate 2009 H1N1 vaccine or funds to support vaccination campaigns in less developed countries

Effectiveness of Antiviral Drugs in Reducing Influenza Associated Illness and the Risk of Severe Complications

- CDC's recommendations for the use of influenza antiviral medications are based on randomized trials that indicate these drugs are effective in reducing the duration of influenza illness by one day among healthy people with mild illness, as well as studies that have consistently found that influenza antiviral treatment reduce the risk of developing serious influenza-associated complications, including deaths among those with severe illness.

    - For treatment, antiviral drugs work best if started within the first 2 days of symptoms. However, studies of hospitalized persons indicate that treatment can also decrease the risk of death and length of hospitalization if started more than 2 days after illness onset.

- Expert panels convened by the World Health Organization (WHO) and CDC agree that there are sufficient data to indicate that antiviral treatment provides substantial benefit for people with influenza illness, especially for people with severe influenza-associated complications that require hospitalization.

- The Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics (AAP) and other groups of medical professionals have also reviewed the evidence of the benefit of antiviral medications and have provided recommendations similar to those from CDC for the use of antiviral medications in the United States.

<u>Effectiveness of antiviral treatment for people with seasonal influenza</u>

- Several randomized, placebo controlled trials (often viewed as the best type of study design in clinical research) have been conducted among outpatients with uncomplicated seasonal influenza illness. These studies found that compared with placebo, antiviral treatment, when started within 48 hours of illness onset, was associated with a reduction in illness severity and approximately 1 day in the duration of illness.

- No randomized trials of oseltamivir or zanamivir treatment of hospitalized patients with influenza illness have been conducted.

    - Because of ethical considerations, it is not appropriate to conduct trials where some patients would receive placebo to determine the

effectiveness of antiviral medications in preventing severe, real-world influenza-associated outcomes, such as hospitalization.

- However, a study by Kaiser et al published in the *Archives of Internal Medicine* which combined results from placebo-controlled clinical trials in adult and adolescent outpatients showed that antiviral treatment was associated with a reduction in lower respiratory tract complications.
    - Also, a randomized placebo-controlled study among outpatient children younger than 12 years of age by Whitley et al published in the *Pediatric Infectious Diseases Journal* showed a reduction in ear infections and antibiotic prescriptions.
- In addition, three observational studies suggest that oseltamivir treatment of hospitalized patients with seasonal influenza reduces the risk of death, and two of these studies show a reduced risk of death even if treatment is started more than 48 hours after illness onset.
    - A Canadian study by McGeer et al published in *Clinical Infectious Diseases* among hospitalized patients with seasonal influenza found that compared to untreated patients, treated patients had significantly lower risk of death within 15 days after hospitalization.
    - A Hong Kong study by Lee et al published in *Clinical Infectious Diseases* among hospitalized patients with influenza illness found that compared to no treatment, treatment was associated with lower mortality if treatment was initiated within 96 hours after influenza illness onset.
    - A retrospective chart review by Hanshaoworakul et al published in *PLoS One* among hospitalized seasonal influenza patients found that compared to no treatment, oseltamivir treatment was significantly associated with survival.

<u>Effectiveness of antiviral treatment for people with severe 2009 H1N1 illness</u>

- Studies examining the effect of neuraminidase inhibitors antiviral medications (oseltamivir [trade name Tamiflu®] and zanamivir [trade name Relenza®]), in reducing complications, including death, among hospitalized patients with 2009 H1N1 consistently show a benefit and have recently been summarized by Dr. Tim Uyeki in the *New England Journal of Medicine* (Link: http://h1n1.nejm.org/?p=1188).
- Observational data from the United States and Mexico suggest that treating hospitalized 2009 H1N1 patients with neuraminidase inhibitors (primarily oseltamivir) may reduce disease severity and mortality.
    - A study by Jain et al published in The *New England Journal of Medicine* found that starting treatment with a neuraminidase inhibitor (e.g.,

oseltamivir or zanamivir) within 2 days after symptom onset was significantly associated with a lower risk of intensive care unit (ICU) admission or death in hospitalized 2009 H1N1 patients.

- A study by Dominguez-Cherit et al published in the *Journal of the American Medical Association (JAMA)* found that among ICU patients with 2009 H1N1, survivors were more likely to have received neuraminidase inhibitor treatment than those who died.

- Although data are limited, these findings from observational studies all suggest the benefits of neuraminidase inhibitor treatment for hospitalized patients.
- CDC continues to recommend antiviral treatment of all hospitalized patients with influenza, including those with pneumonia

2009 H1N1 Influenza Vaccine

In this Section:

- Announcements
- Supply
- Recommendations
- Flu Activity Occurs in Waves

Announcements

- National Influenza Vaccination Week (NIVW) is a national initiative that was established to highlight the importance of continuing influenza vaccination, as well as to foster greater use of flu vaccine after the holiday season into January and beyond. This year's NIVW, originally scheduled for December 6-12, 2009, is now rescheduled to January 10-16, 2010. Updates will be provided as more information becomes available.
- We hope that all of our partners will plan their own NIVW events and share their plans with us at www.flu.gov and http://www.cdc.gov/flu/NIVW/form.htm.
- **(New)** Webcast for Health Care Providers: Join us December 16, 12-1 pm ET, as experts from the U.S. Department of Health and Human Services and the former president of the American Medical Association answer your questions about the 2009 H1N1 virus and vaccine. The webcast is hosted by the HHS and will be live on www.flu.gov. Join the discussion by sending questions or comments to hhsstudio@hhs.gov.
- **(Updated)** HHS has joined with the Ad Council to launch a new nationwide Public Service Announcements (PSA) campaign called

Together We Can All Fight the Flu that encourages Americans to get vaccinated against the 2009 H1N1 flu virus. The PSAs are now available for various audiences at www.flu.gov.

- CDC has received reports of fraudulent emails (phishing) referencing a CDC sponsored State Vaccination Program. The messages request that users must create a personal 2009 H1N1 (swine flu) Vaccination Profile on the cdc.gov web site. The message then states that anyone that has reached the age of 18 has to have his/her personal Vaccination Profile on the cdc.gov site. The CDC has **NOT** implemented a state vaccination program requiring registration on www.cdc.gov. Users who click on the email are at risk of having malicious code installed on their system.

Supply

- On November 16, 2009, the Food and Drug Administration (FDA) announced its approval of a fifth vaccine for protection against the 2009 H1N1 flu virus. This vaccine will be manufactured using the same established, licensed egg-based process that is used for producing seasonal flu vaccine and will be produced in multi-dose vials, in a formulation that contains thimerosal. Since this vaccine will not be available for distribution until the end of December, it does not affect current vaccine supply.

- **(Updated)** As of Friday, December 11, 2009, a total of **86,844,500** doses were available for ordering. Of those available doses, 67,132,900 doses were injectable (flu shots) and 19,711,600 were LAIV (nasal spray vaccine).

- **(Updated)** As of Thursday, December 10, 2009, there were a total of 78,017,600 doses ordered.

- The further delivery of Sanofi Pasteur 7.5 microgram prefilled syringes is delayed indefinitely due to release issues at the manufacturer.

- Supplies of 2009 H1N1 vaccine continue to increase. More doses are expected for shipment each week. We ask members of the public who want to receive this vaccine to be patient as this program expands and more vaccine continues to become available.

Recommendations

- Parents are now encouraged to seek the second dose of 2009 H1N1 vaccine for their children who are younger than 10 years old. The recommended interval between the first and second dose should be at least 28 days, however, a second dose given at least 21 days after the first is considered valid.

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Flu Activity May Occur in "Waves"

- The timing, spread and severity of influenza viruses is uncertain.
- Outbreaks of influenza may occur in different places at different times.
- Outbreaks may occur in waves of about 6-12 week time periods.
- These waves of influenza may occur over a year or so after the emergence of a new influenza virus.
- In past pandemics, "waves" of activity have been observed.
- The first wave is usually a smaller wave; followed by a larger "peak" wave. Subsequent smaller waves can occur as well.
- The United States experienced its first wave of 2009 H1N1 pandemic activity in the spring of 2009.
- At this time, we are experiencing a second wave of 2009 H1N1 activity.
- It's possible that other waves of influenza activity may occur after this current wave – caused by either 2009 H1N1 viruses or regular seasonal flu viruses.
- Because the timing and spread of influenza viruses are unpredictable, CDC is continuing to recommend vaccination with seasonal influenza vaccine and 2009 H1N1 vaccine for those people in whom it is recommended.

2009 H1N1 Influenza Vaccine Safety

- Getting the 2009 H1N1 influenza vaccine is much safer than getting H1N1 influenza. You can prevent 2009 H1N1 influenza illness by getting the 2009 H1N1 vaccine.
- The benefits of getting the 2009 H1N1 influenza vaccine far outweigh the very small risk of serious complications from vaccination. Some people getting vaccinated will have mild side effects such as pain, redness or swelling in the arm where the shot was given or a runny nose and headache after the nasal spray vaccine.

MMWR: Monitoring the Safety of Influenza A (H1N1) 2009 Monovalent Vaccines in the United States, Preliminary Findings

- In this MMWR, published December 4, 2009 CDC reports on the preliminary safety results for the 2009 H1N1 influenza vaccines from the first months of reports received through the U.S. Vaccine Adverse Event Reporting System (VAERS), a national surveillance system and data from the Vaccine Safety Datalink.

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- The VAERS database was searched to identify all U.S. reports received of adverse events following vaccination with 2009 H1N1 vaccines and 2009 seasonal influenza vaccines from July 1, 2009 through November 24, 2009.

- Data from VAERS show that in post-licensure monitoring, the overall reporting rate after 2009 H1N1 vaccination is higher than that for seasonal influenza vaccination. Although this might represent an actual difference in safety, increased reporting rates are expected due to the efforts to enhance reporting to VAERS and the heightened public awareness of the 2009 H1N1 vaccine.

- As of November 24, 2009, nearly 52 million doses of 2009 H1N1 vaccine had been shipped to vaccination providers in the United States.

- As of November 24, 2009, VAERS had received 3,783 adverse event reports following 2009 H1N1 vaccination.

- The vast majority (95%) of adverse events reported to VAERS after receiving the 2009 H1N1 vaccine were not serious (e.g., soreness at the vaccine injection site).

- Of the 3,783 reports, 204 (5%) were reports that involved what would be considered serious health events (defined as life threatening or resulting in death, major disability, abnormal conditions at birth, hospitalization, or extension of an existing hospitalization).

- The percentage of reports involving what would be considered serious health events is not substantially different between 2009 H1N1 and seasonal influenza vaccines. Additionally, no new or unusual events or pattern of adverse events have emerged. VAERS reports continue to be monitored as more vaccine is administered.

- Among the 204 reports of serious health events after H1N1 vaccination, there were 13 reports of death.

- The 13 VAERS reports that involve deaths are under review by CDC, FDA and the states where the reported deaths occurred. Preliminary findings do not indicate a common cause or pattern (such as similarities in age, gender, geographic location, illness surrounding death, or underlying medical conditions) to suggest that these deaths were associated with the vaccine. These cases are under further review pending additional medical records (e.g. autopsy reports, medical files).

- VAERS received 10 reports of Guillian-Barré syndrome (GBS) of which follow-up assessments are underway. An additional 2 reports describing

neurologic events are also under review as possible GBS. In the United States, about 80-160 cases of GBS are expected to occur each week, regardless of vaccination.

- Eleven (11) reports of anaphylaxis were received by VAERS; an additional 8 reports of possible anaphylaxis were identified. Of these 19, 13 met Brighton Collaboration case definition criteria, five had an anaphylaxis diagnosis on medical record review, and one has not been confirmed. These 19 reported cases of anaphylaxis are not at a rate above the background rate for this adverse event.

- CDC has enhanced vaccine safety monitoring efforts in several ways:

    - The Vaccine Adverse Event Reporting System (VAERS) is a voluntary reporting system that identifies potential vaccine safety signals: healthcare providers are actively reminded to report clinically significant adverse events after vaccination, even if they are not sure if the vaccine caused the adverse event, and medical personnel are conducting daily reviews and follow-up [http://vaers.hhs.gov].

    - Second, a new Web-based active surveillance system is being implemented to prospectively follow tens of thousands of vaccinated people [www.myflushot.org].

    - Third, large population-based systems that link computerized vaccination data with healthcare codes are being used to conduct rapid and ongoing analyses. This approach includes data from large managed care plans, other health plans, Department of Defense, Medicare and the Veterans' Administration.

    - Fourth, active case finding for Guillain-Barré syndrome (GBS) is being conducted in 10 areas of the United States (a combined population of about 45 million people).

- Findings from all sources are cross-referenced and reviewed by government and outside scientists to be sure any concerns are rapidly addressed.

In this Section:

Seasonal Influenza Vaccine

- Two systems that look at seasonal influenza vaccinations administered and billed show that more individuals have been vaccinated with seasonal vaccine this season than at the same time last year. This is most likely

due to the early availability of vaccine and public interest in getting vaccinated.

Seasonal Influenza Vaccine Supply and Distribution

- Due to early availability and high demand of seasonal flu vaccine, limited amounts of seasonal supply remain. At this point, CDC continues to encourage those at highest risk from flu complications to seek seasonal flu vaccine and receive 2009 H1N1 vaccine, as recommended.
- As of November 27, approximately 104.8 million doses of seasonal influenza vaccine have been distributed. This is 91% of the doses expected this season.
- Local areas may not have received as much vaccine as they anticipated at this point in the season and providers seeking additional vaccine now may be unable to purchase it. For more information about seasonal supply, please refer to IVATS (http://www.preventinfluenza.org/ivats/) over the coming weeks.

More information about seasonal flu vaccine supply can be found at:
http://www.cdc.gov/flu/professionals/vaccination/#supply